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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/170,980	10/13/98	HILLMAN J	PF-0195-1DIV

HM12/0330

INCYTE PHARMACEUTICALS INC
PATENT DEPARTMENT
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EXAMINER	
EYLER, Y	
ART UNIT	**PAPER NUMBER**
1642	7

DATE MAILED: 03/30/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File Copy

Office Action Summary	Application No. 09/170,980	Applicant(s) Hillman et al.
	Examiner Yvonne Eyler	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Jan 13, 2000* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 11-16, and 18-24* is/are pending in the application.

Of the above, claim(s) *11-16 and 21-24* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1 and 18-20* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I in Paper No. 5 is acknowledged. The traversal is on the ground(s) that it would not require an undue burden to search groups I-IV together because the searches would overlap. Applicant further argues that Group V should have been search and examined in the parent case and therefore would not require undue burden to search and examine instantly. This is not found persuasive because each of the groups are to substantially different inventions which require different searches that are not required for any other Group. While a single facet of search may overlap, the majority of the search and considerations involved in the examination of each Group are unique, as exemplified by the different classifications.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1 and 18-20 are under consideration in the application. All other claims are withdrawn from further consideration as being drawn to a non-elected Group of invention.

Specification

The disclosure is objected to because of the following informalities:

The continuing data on the first line of the specification should be updated to indicate the current status of the parent application.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

Claim Rejections - 35 USC § 112

2. Claims 1 and 18-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to isolated polypeptides and fragments comprising SEQ ID NO: 1, as well as pharmaceutical compositions comprising the polypeptides.

The specification contemplates the use of the compounds for either diagnosis or treatment of HPAK associated diseases.

The specification discloses a polypeptide consisting of SEQ ID NO: 1 and demonstrates sequence shares regions of homology with human pancreatic kallikrein and shares an amino acid residue D200 which is contemplated to be likely to confer chymotrypsin-like activity. The specification also contemplates an association with the development of cancer based on the detection of transcripts from prostate cancer tissues. The specification further contemplates detection of HPAK to be indicative of disorders such as asthma, prostate cancer, parotid gland cancer, and breast cancer.

The instant specification fails to provide a specific utility for the instantly claimed polypeptides. There is no description of the chemical, physical, or biological properties for polypeptides other than the sequence. Shared homologies with other polypeptides does not

provide a disclosure of a specific utility for the instant polypeptide being claimed nor does the ability to determine if the polypeptide possess protease activity support a use dependent on that potential activity. Further, no predictable correlation of the expression of the instant polypeptides with a specific disease is provided, other than the detection in prostate cancer tissue, which is unpredictive of an association with cancer since the polypeptide may be expressed in prostate tissue in general. There is no objective evidence provided supporting specificity of expression of the polypeptide and diagnosis of any disease state. Additionally, there is no art of record that discloses or suggests any activity for the claimed protein. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed amino acid sequence. Therefore, the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above.

3. Claims 1 and 18-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

4. Claims 1 and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "naturally-occurring amino acid sequence" found in claim 1 is vague and indefinite because the metes and bounds of the claimed polypeptide cannot be determined. The

specification on page 4 discloses that the recitation is not meant to limit to a complete, native sequence. The specification does not provide any further guidance with regard to what the recitation is meant to limit to. The definition of what a compound is not does not clearly and concisely set forth what that compound is.

The recitation of "biologically-active fragment" of SEQ ID NO: 1 is vague and indefinite because the metes and bounds of the claimed polypeptide or fragment cannot be determined. The specification on page 5 defines biologically active as having structural, regulatory, or biochemical functions of a naturally occurring molecule. As noted above, a naturally occurring molecule is vague and indefinite and cannot be identified. Further, the specific, identifiable, measurable actions that are considered to be structurally, regulatory, or biochemically definite of the polypeptide are not set forth such that one of skill in the art would be able to unequivocally identify the encompassed polypeptides claimed. Likewise the term "immunologically-active" is defined as the ability to induce an immune response or bind to antibodies in an appropriate cell or animal, yet the factors determining appropriate are not set forth. It is further noted that the specification does not provide strict, technical support for the instantly claimed "antigenically-active fragment."

The recitation of a "suitable pharmaceutical carrier" is vague and indefinite because it is not clear what it is suitable for.

5. Claims 1 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification discloses a single species of polypeptide comprising SEQ ID NO: 1. The instant specification does not, however, contain a written description of the invention encompassed by naturally-occurring sequences having 90% identify, polypeptides comprising biologically-active fragments or polypeptides comprising antigenically-active fragments in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The claims, as written, however, encompass polypeptides which vary substantially in length and also in amino acid composition. The specification and claims do not indicate common structural and functional attributes shared by the members of the broadly claimed genus such that the members may be identified. The specification proposes to identify other members of the genus by determining similar biological, immunological, or enzymatic activities, which activities are not described. There is also no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of a single specific

amino acid sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

6. Claims 1, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for substantially purified polypeptides comprising SEQ ID NO: 1 and a composition comprising the polypeptide of SEQ ID NO: 1 and a pharmaceutically acceptable carrier, does not reasonably provide enablement for any polypeptides comprising functional fragments or homology to SEQ ID NO: 1 or pharmaceutical compositions comprising them. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The specification discloses an amino acid sequence, SEQ ID NO: 1. The specification fails to provide guidance or objective evidence regarding the identifying activities of the amino acid sequence or the structural features of the amino acid sequence that are critical to its function.

The amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be substituted within a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of this protein are lacking, as well as detailed guidance regarding its definitive activity, it is unpredictable as to which amino acid substitutions and which fragments of the sequence, if any, meet the limitations of the claim. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of substituted proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. Therefore, one of ordinary skill would require guidance, such as information regarding the extent of substitution and the location and the specific amino acid changes which would result in the preservation of the stated activity. Therefore, it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

With regard to the pharmaceutical compositions of claims 19 and 20, the language pharmaceutical composition connotes *in vivo* applicability of the composition for achieving therapeutic effect. There is insufficient objective evidence provided, however, to render such an effect predictable. There is insufficient objective evidence regarding a predictable correlation between a reduction in expression or activity of the instant amino acid sequence and development of a disease that would be ameliorated upon restoration of the polypeptide. There is additionally

no disclosure of a specific activity of the amino acid sequence which upon administration to a patient would predictably result in amelioration of a given disease. Absent objective evidence to the contrary, it would require undue experimentation for one of skill in the art to utilize the instant amino acid sequence, or any other sequence comprising fragments of the instant sequence, in a pharmaceutical composition to treat an disease. Further, it would require undue experimentation for one of skill in the art to make and/or use the full scope of the claimed invention as detailed above.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

8. Claims 1 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al. (EP 297 913-IDS 11).

Lin et al. teach a polypeptide having 99.6% identity to the instant SEQ ID NO: 1, differing in a single amino acid residue. Lin et al. further teach the use of pharmaceutical compositions comprising the polypeptide to successfully lower blood pressure. See Lin et al., page 13 and 31.

9. Claims 1 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Shine et al. (WO 87/02709-IDS 12).

Shine et al. teach a polypeptide having 99.2% identity to the instant SEQ ID NO:1 and formulation for reduction of hypertension.

10. Claims 1 and 18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Au-Young et al. (U.S. # 5,869,637) or Bandman et al. (U.S.# 5,786,148).

Au-Young et al. teach a kallikrein that is 100% identical to the instant polypeptide of SEQ I D NO: 1 and teach pharmaceutical compositions comprising the polypeptides.

Bandman et al. teach a kallikrein polypeptide having 99.6% identity to the instant SEQ ID NO: 1 and pharmaceutical compositions comprising the polypeptides.

11. Claims 1 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by each of Evans et al. (Biochemistry 27:3124-3129, 1988), Baker et al. (DNA 4:445-450, 1985), Angermann et al. (Biochem J. 104:22-29, 1988), or Lu et al. (Int. J. Pep. Protein Res. 33:237-249, 1989).

Each of Evans et al, Baker et al., Angermann et al., and Lu et al. teach a polypeptide having 100% identity to the instant SEQ ID NO: 1.

NO CLAIM IS ALLOWED

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yvonne Eyler, Ph.D. whose telephone number is (703) 308-6564. The examiner can normally be reached on Monday through Friday from 830am to 630pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[paula.hutzell@uspto.gov]**.

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler

Yvonne Eyler, Ph,.D.
Primary Examiner
March 25, 2000